Assessment of the extent of microcalcifications to predict the size of a ductal carcinoma in situ: comparison between tomosynthesis and conventional mammography

Berger, Nicole ; Schwizer, Sibylle Dubach ; Varga, Zsuzsanna ; Rageth, Christoph ; Frauenfelder, Thomas ; Boss, Andreas

Abstract: OBJECTIVES The objective was to determine if digital tomosynthesis of the breast (DBT) assesses the extension of ductal carcinoma in situ (DCIS) with higher precision than mammography (MG). MATERIAL AND METHODS The local ethics committee approved this retrospective study including 26 patients with DCIS, which were rated by three radiologists. Statistics were performed using intraclass correlation (ICC) for interreader agreement and the Pearson correlation for correlation of MG and DBT. Standard of reference was the histologic extension. RESULTS The ICC was excellent. Correlation between MG and histology was 0.879 (P<.01) and for DBT and histology was 0.914 (P<.01). CONCLUSION DBT provides a slightly better estimation of the size of a DCIS than MG.

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Assessment of the extent of microcalcifications to predict the size of a DCIS: Comparison between tomosynthesis and conventional mammography

-Original Research-

Nicole Berger, MD[1,2], Sibylle Dubach Schwizer, MD[2], Zsuzsanna Varga, MD[3], Christoph Rageth, MD[2], Thomas Frauenfelder[1], MD, Andreas Boss, MD, PhD[1];

[1] Institute of Diagnostic and Interventional Radiology, University Hospital Zurich, Raemistrasse 100, 8091 Zurich, Switzerland (nicole.berger@usz.ch; thomas.frauenfelder@usz.ch; andreas.boss@usz.ch)
[2] Breast Center Zurich, Seefeldstrasse 214, 8008 Zurich, Switzerland (s.dubach@brustzentrum.ch; c.rageth@brust-zentrum.ch)
[3] Institute of Surgical Pathology, University Hospital Zurich, Raemistrasse 100, 8091 Zurich, Switzerland (zsuzsanna.varga@usz.ch)

Corresponding Author:
Nicole Berger, MD
Institute of Diagnostic and Interventional Radiology
University Hospital Zurich
Raemistrasse 100
CH – 8091 Zurich
Switzerland
Tel: +41 44 255 1111
Fax: +41 44 255 4443
E-mail: nicole.berger@usz.ch

Abstract

Objectives

If digital tomosynthesis of the breast (DBT) assesses the extension of Ductal carcinoma in situ (DCIS) with higher precision than mammography (MG).

Material and Methods

Retrospective and local ethic committee approved study including 26 DCIS, which were rated by three radiologists. Statistics were performed using intraclass correlation (ICC) for inter-reader agreement and the Pearson's Correlation for correlation of MG and DBT. Standard of reference was the histologic extension.

Results

The ICC was excellent. Correlation between MG and histology was 0.879($p<0.01$) and for DBT and histology 0.914($p<0.01$).

Conclusion

DBT provides a slightly better estimation of the size of a DCIS than MG.

Key words: DCIS; Tomosynthesis; Mammography; Microcalcification; Breast;

1. Introduction

Ductal carcinoma in situ (DCIS) is a noninvasive breast cancer originating from the ducts of the breast [1]. DCIS is treated the same way as invasive breast cancer with surgical excision and radiotherapy and if needed hormonal therapy as it is able to progress into invasive breast cancer [2]. It has a similar recurrence rate like invasive cancer in 10 years if only treated by resection without radiotherapy compared to a combined therapy [3]. Nevertheless a total surgical resection of the DCIS with absence of the tumor in the remaining tissue (R0) is aimed [4]. An even higher recurrence rate occurs, if an extensive intraductal component (EIC) of an invasive breast cancer is found [5]. Grouped microcalcifications in mammograms (MG) and digital tomosynthesis of the breast (DBT) are the best signs of a potentially underlying DCIS or an invasive cancer. Further examinations like a core needle biopsy or vacuum-assisted biopsy are needed for clarification or exclusion of malignancy [6]. However in up to 40% (mostly in low grade DCIS) no calcifications can be seen [7].

MG is performed in two planes (cranio-caudal CC and medio-lateral-oblique MLO views). Although they are not performed in a right angle to another, it allows a full capture of breast tissue and anatomical localization of lesions. Dense breast tissue and the lacking of the third dimension might hamper the exact localization of the lesion. Compared to MG, DBT gives a three dimensional (3D) aspect of the underlying tissue by imaging the breast in thin slices so that tissue is not superimposed [8]. In most cases DBT is acquired in the same two planes as MG (CC and MLO). Newer studies point out that two DBT planes are not always necessary if MG has been performed in two planes [9]. Still DBT helps to improve diagnostic accuracy of detection of breast lesions compared to mammography alone [10, 11].

In our clinical routine, often an estimation of the dimension of a DCIS is done, before surgical treatment by measuring the size of the grouped microcalcifications on MG, if no magnetic resonance imaging (MRI) of the breast has been performed [12]. In the current study, we investigate whether the 3-dimensional information of DBT has an impact on the accuracy of tumor size estimation of DCIS compared to MG.

2. Methods

2.1 Study population

The study was approved by the local ethics committee. A retrospective text search for DCIS was made in the patient database from January 2010 to June 2015 in our Breast Center and 213 patients with a DCIS were found. Inclusion criteria were MG of the affected breast in two views mediolateraloblique (MLO) and craniocaudal (CC), and DBT had to be performed in at least one view (CC or MLO or both). Further, a total surgical resection with complete histologic analysis of the tissue proving DCIS had to be carried out. Thirty-two patients with 33 DCIS were found. Seven patients were excluded due to a large non-calcified part of the DCIS (defined as more than 5 cm in the histologic examination). The final study population included 26 patients with 26 DCIS (Table 1).

2.2 Image acquisition protocol

MG and DBT of the breast were performed on a Hologic Selenia Dimensions 3D mammography system (Marlborough, MA, USA) without using the combo-mode as first the MG were acquired and if required in a second step the DBT was performed.

2.3 Image interpretation

Interpretation of the data was performed on a PACS workstation equipped with a dedicated breast imaging reading software (AGFA Impax 6, Mortsel, Belgium). One radiologist (XY) rated the image quality of the included MG and DBT examinations according to the ACR-guidelines [13]. Three radiologists XX, XY and YY (blinded for review) with 12, 6 and 20 years of experience in breast imaging evaluated MG and the whole volume of the DBT independently and in a non-chronologic order. The radiologists were blinded to the definitive pathologic report but were aware of a present DCIS in the exams. No previous images were accessible for comparison. Three exams of 33 had only one plane in DBT and the slice thickness of the DBT was set at 1 mm. Each radiologist rated the data according to Table 2 (Figure 1 and 2) and measured the maximal extension of the microcalcifications in [mm]

(either in CC or MLO) in MG and on a selected slice of the DBT with the largest extension according to the radiologist. Moreover, suspicion of multifocality and multicentricity of the DCIS were evaluated. No time limit was set or recorded, but the radiologists were asked after the evaluations, which method MG or DBT required more time.

2.4 Statistical analysis

Association between measurements and histologic proven size of DCIS were calculated using the Pearson's Correlation. A p-value of <0.01 was defined as statistically significant. The histologically measured extend of the tumor served as standard reference. Intraclass correlation was calculated for reader's agreement with values less than 0.40 being poor, fair for values between 0.40 and 0.59, good for values between 0.60 and 0.74, and excellent for values between 0.75 and 1.0 [14, 15]. Statistical analyses were performed using SPSS (Version 17.0, IBM, Chicago, USA). Linear regression and the Bland-Altman plot [16] were performed on GraphPad Prism (Version 5, San Diego, California).

3. Results

All 33 MG and DBT of the DCIS were of good image quality. No examination had to be excluded. Typical image quality of MG and DBT can be assessed in Figure 1 and 2 with examples of the measurements of the extent of the microcalcifications. Histological sizes of DCIS ranged between 1 and 124 mm (median 20 mm). Intraclass correlations (ICC) of the three readers were both excellent for MG 0.923 and for DBT 0.912 ($p<0.001$). Regarding the good consensus of the readers and the nearly identical correlation coefficients, the statistical plot is only shown for reader XX (Fig 3-5).

Correlation between MG and histology was 0.879 (for reader XX), 0.717 (for reader XY) and 0.735 (for reader YY) and between DBT and histology 0.914 (for reader XX), 0.783 (for reader XY) and 0.770 (for reader YY) ($p< 0.001$) showing that by using DBT the estimation of the extension of a DCIS is better than by using MG. Plots of the extension of the calcifications in MG and DBT versus the histology reference standard for reader XX (Fig

3) are provided in Fig. 4 and 5; furthermore the respective linear regression lines are depicted. The extension in histology compared to MG was 19.7% larger; therefore, the definitive size was underestimated by 16.5% (accumulated error of 11.5%). The extension in histology compared to DBT was 17.9% larger; consecutively the definitive size was underestimated by 15.2% (accumulated error of 9.1%). A Bland-Altman plot (Fig 6) was calculated to show that all measurement points between MG and DBT except three are within the ± 1.96 standard deviation of the mean paired differences.

Multifocality

Only 3 of 32 patients had a multifocal DCIS and two of them were rated to be multifocal in MG and DBT by all readers. One of the multifocal DCIS was not rated multifocal by all readers due to a part of this particular DCIS without calcifications. Multifocality was overestimated by all readers by rating 3 to 12 of 33 DCIS cases as multifocal. None of our cases were DCIS without any calcifications.

Multicentricity

Only 1 of 33 DCIS was multicentric. This case was missed by all readers because parts of this DCIS showed no calcifications.

Invasive component

Only 2 of 33 DCIS showed an invasive component with one of them being rated as positive for an invasive component by all readers. Up to 16 cases in MG were rated by one reader to have a suspected invasive component. Therefore the feature of an underlying invasive carcinoma was highly overrated. In DBT the invasive component was rated positive in fewer cases (max. 11 of 33 by one reader).

4. Discussion

In the present study we found that DBT provides a slightly better estimation of the histological extension of DCIS compared to MG, which may be ascribed to the 3-dimensional representation of the breast lacking the superimposition of breast tissue on projection views. However, the time to reliably read a DBT is notably longer compared to MG which

concurrent with previously published studies [17]. Moreover, assessment of invasive components, multifocality, and multicentricity remains challenging even in DBT. One reader highly overestimated the invasive component especially in mammography due to supraposition of glandular tissue, with much less DCIS rated invasive by using DBT, where the supraposition of glandular tissue decreases. The one invasive cancer, which was missed by all three readers didn't show any visible mass to be rated invasive and histologically with only a small invasive part.

Both, MG and DBT may result in underestimation of the extent of DCIS for DCIS exhibiting substantial non-calcified areas, especially in the non-high grade lesions.

R0-resection could be performed based on the preoperative measurements of the extension of the grouped microcalcifications in 28 of 33 cases, showing that in the majority of cases extent of the microcalcifications provide a reasonable estimate of the true extension of the DCIS. Nevertheless with evaluating the microcalcifications the real size is underestimated by about 16.5% in MG and a little less with 15.2% in DBT. Based on this finding, we suggest both methods are applicable in the daily use if no MRI images are available preoperatively as MRI often overestimates an underlying DCIS. Preoperative MRI often leads to a more extensive surgery [18] and a preoperative MRI is; therefore, in our clinical setting rarely applied. However there are cases, where an extension of the resection or a re-excision might become necessary if positive margins remain [19]. Not fully resected DCIS could be on the basis of non-calcified areas, which are mentioned in the literature to be up to 40% [7]. In the estimation of the DCIS extent, DBT shows slightly higher accuracy compared to MG at, however, longer reading time [20].

Our study had some limitations. First, the study was a retrospective investigation and it was performed at a single center. Only proven and resected DCIS were included which might have led to a selection bias. Also the radiologists knew of the presence of at least one DCIS in the presented images as no negative images were evaluated. Third as DCIS not mandatorily show microcalcifications, the measurements of the extensions of the microcalcifications have

not always reflected the whole extension of the lesion. Therefore 6 patients were removed as outliers from the calculation of correlation of the measurements and the definitive histological extension of the DCIS when large non-calcified parts of DCIS were proven in histology. Third a compression of the breast might also influence the rated extension of the microcalcifications due to the loss of the real underlying three-dimensional extension.

5. Conclusion

This study shows that DBT is statistically slightly better to determine the size of a DCIS using the extent of the microcalcifications compared to MG. Overall using MG or DBT, both adequately can be used to estimate the approximate size of the DCIS. Nevertheless regions of a DCIS without microcalcifications have to be kept in mind, which might lead to an underestimation of the final lesion.

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Tables

Table 1

Patient demographics including age, pre- and postmenopausal status, grade of DCIS, occurrence of lymph nodes metastases and breast density (ACR).

Total number of patients	32
Treated Ductal Carcinoma In Situ (DCIS)	33
Age [years]	60 ± 11
Pre-menopausal	10
Postmenopausal	22
High grade DCIS	15
Low grade DCIS	13
Mixed DCIS (high and low grade)	5
Sentinel node positive	0
ACR* a	6
ACR b	11
ACR c	13
ACR d	3
Total resection after first operation	28

*Breast density (ACR)

Table 2

List of read out criteria for MG and DBT either measuring in [mm] or rating yes/no [y,n] or the shape of microcalcifications monomorph/polymorph [m/p].

Criteria	
Maximal extension of the microcalcifications	[mm]
Multifocality	[y,n]
Multicentricity	[y,n]
Adjacent invasive component	[y,n]
Shape of microcalcifications	[m/p]

Figures

Figure 1

Left image A: Microcalcifications in MG are marked with a circle and the maximal extension was measured. B: Microcalcifications in DBT (four images with a space of 3 mm between each other). The extension of the microcalcifications is marked and with arrows (slice thickness was set to 1 mm).

Figure 2

A: Example of measurement of the extension of the microcalcifications in MG (17 mm, depicted by the dotted line). B: Example of measurement of the extension of the microcalcifications in BDT (24 mm, depicted by the dotted line). The histological extension of the DCIS was 32 mm.

Figure 3

A: Hematoxylin eosin (HE) stain of the according low-grade micropapillary DCIS (magnification 25X). B and C: HE stain of the corresponding low-grade cribriforme DCIS with comedo like necrosis and associated calcification (C: magnification 10X, D: magnification 25X). The final maximal extension in the histology was measured to be 35 mm.

Figure 4

Measured extensions of the calcifications in the MG compared to the real extension of the DCIS in the histology. The correlation coefficient was 0.872. Solid line: Linear regression line, y = 1.197x +2.868. Dotted line: identity line.

Figure 5

Measured extensions of the calcifications in the DBT compared to the real extension of the DCIS in the histology. The correlation coefficient was 0.917. Solid line: Linear regression line, $y = 1.179x + 3.081$. Dotted line: identity line.

Figure 6

Bland-Altman plot of the differences of the two measurement methods (MG and DBT) of the extension of the microcalcifications and the average. Three measurements are overlapping. Except three measurement points all other are within the ± 1.96 standard deviation of the mean paired differences.

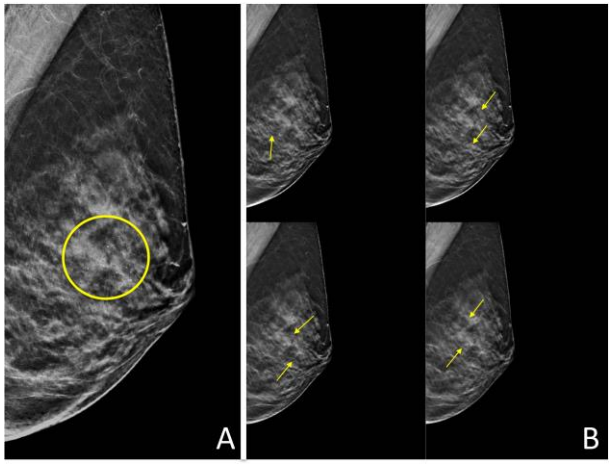

Figure 1

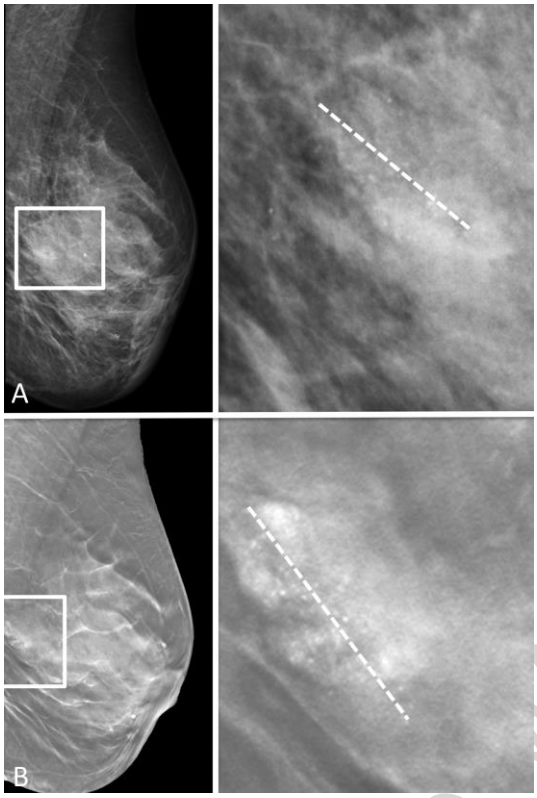

Figure 2

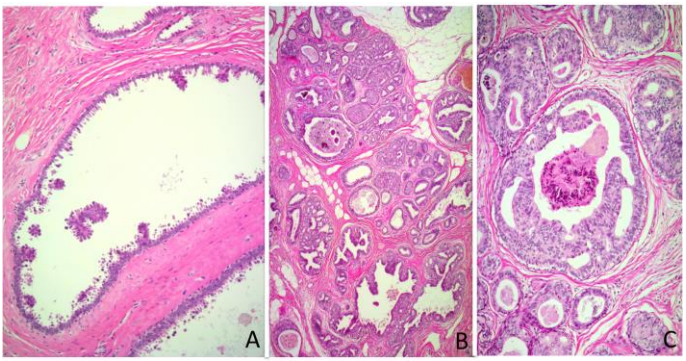

Figure 3

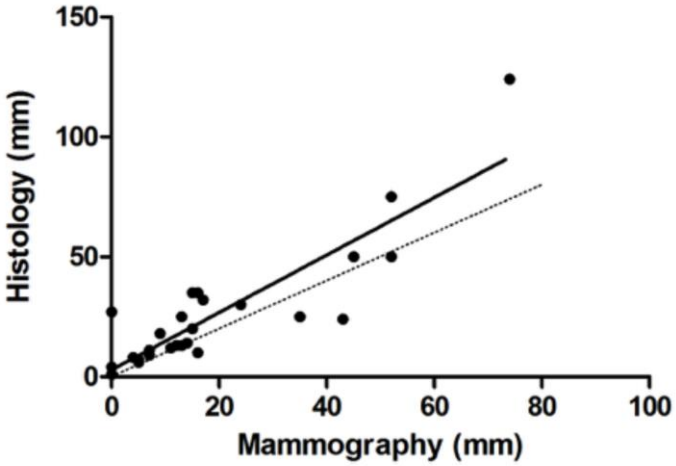

Figure 4

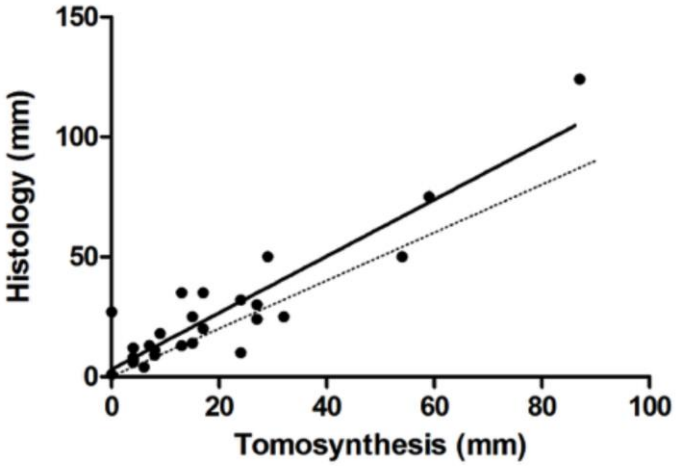

Figure 5

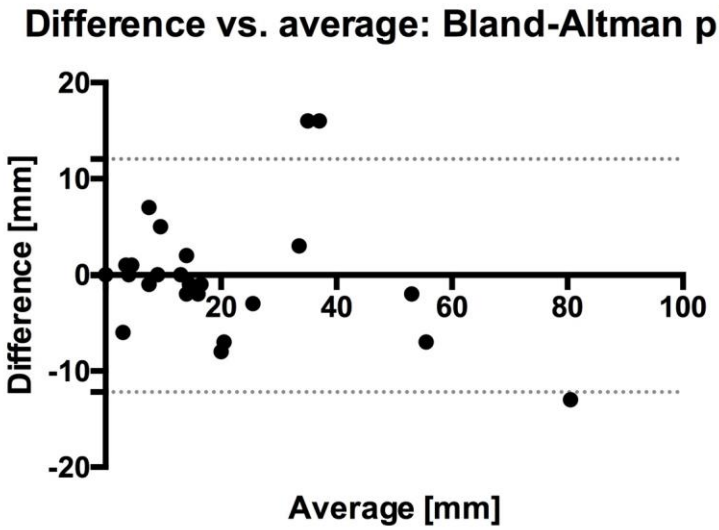

Figure 6